

THAT WHICH IS CLAIMED

1. A method for modulation of an immune response of an organism, said method comprising contacting said organism with a spore system comprising a  
5 recombinant spore having at least one exogenous nucleic acid, peptide, or polypeptide which modulates an immune response in the organism, wherein said spore is administered via a delivery system selected from the group consisting of respiratory delivery system, nasal delivery system, parenteral delivery system, and mucosal delivery system.  
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2. The method of claim 1, wherein said modulation is the production of an immune response.
3. The method of claim 1, wherein said modulation is the enhancement of an  
15 immune response.
4. The method of claim 1, wherein the nucleic acid, peptide, or polypeptide is displayed on or bound to a surface of the spore.
- 20 5. The method of claim 1, wherein the nucleic acid, peptide, or polypeptide is contained within the spore.
6. The method of claim 1, wherein said modulation results from the release of the nucleic acid, peptide, or polypeptide from the spore system.  
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7. The method of claim 1, wherein the spore of said spore system is a non-viable spore.
8. The method of claim 1, wherein the spore of said spore system is a  
30 bacterial spore.

9. The method of claim 1, wherein the at least one exogenous nucleic acid, peptide, or polypeptide comprises at least one immunomodulatory agent.

10. The method of claim 9, wherein said at least one immunomodulatory agent  
5 is selected from the group consisting of: cytokines, co-stimulatory agents, antigens, antibodies, adjuvants, and binding receptors.

11. The method of claim 10, wherein the at least one immunomodulatory agent comprises an antigen.

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12. The method of claim 1, wherein the polypeptide or peptide is produced as a fusion protein with a spore coat protein.

13. The method of claim 12, wherein the spore coat protein is at least one  
15 protein selected from the group consisting of: CotA, CotB, CotC, CotD, CotE, CotF, CotG, CotN, CotS, CotT, CotV, CotW, CotX, CotY, and CotZ.

14. The method of claim 13, wherein the spore coat protein is CotC protein.

20 15. The method of claim 13, wherein the spore coat protein is CotD protein.

16. The method of claim 1, wherein the nucleic acid, peptide, or polypeptide is produced by vegetative cells produced by said spore following germination of said spore.

25 17. The method of claim 1, wherein said spore is delivered via the respiratory delivery system.

18. The method of claim 1, wherein said spore is delivered via the nasal delivery system.

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19. The method of claim 1, where said spore is delivered via the parenteral delivery system.

20. The method of claim 1, wherein said polypeptide is displayed on the surface of the spore after lysis of the mother cell of said spore.

21. A method for modulation of an immune response of an organism, said method comprising contacting said organism with a spore system comprising a non-viable recombinant spore having at least one exogenous nucleic acid, peptide, or polypeptide which modulates an immune response in the organism.

22. The method of claim 21, wherein said nucleic acid, peptide, or polypeptide is displayed on or bound to a surface of the spore.

23. The method of claim 21, wherein said polypeptide is an antigen and said peptide is an antigenic peptide.

24. The method of claim 21, wherein said polypeptide, or peptide is produced as a fusion protein with a spore coat protein.

25. The method of claim 24, wherein said spore coat protein is at least one protein selected from the group consisting of: CotA, CotB, CotC, CotD, CotE, CotF, CotG, CotN, CotS, CotT, CotV, CotW, CotX, CotY, CotZ.

26. A composition comprising a spore system, said spore system comprising a spore and at least one exogenous nucleic acid molecule, peptide, or polypeptide displayed on, bound to, or contained within said spore wherein said nucleic acid, peptide, or polypeptide modulates an immune response when administered to an organism via the respiratory delivery system, nasal delivery system, or the parenteral delivery system.

27. The composition of 26, wherein the nucleic acid, peptide, or polypeptide is displayed on or bound to the surface of the spore.

28. The composition of 26, wherein the peptide or polypeptide is produced as a  
5 fusion protein with a spore coat protein.

29. The composition of 28, wherein the spore coat protein is at least one protein selected from the group consisting of: CotA, CotB, CotC, CotD, CotE, CotF, CotG, CotN, CotS, CotT, CotV, CotW, CotX, CotY, and CotZ.

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30. A composition comprising a spore system, said spore system comprising a spore, at least one antigen, and at least one adjuvant and/or co-stimulatory polypeptide.

31. The composition of claim 30, wherein said at least one antigen is displayed  
15 on or bound to the surface of the spore.

32. The composition of claim 30, wherein said at least one antigen is contained within the spore.

33. The composition of claim 30, wherein said spore of said spore system is a  
20 non-viable spore.

34. The composition of claim 30, wherein said at least one adjuvant or co-stimulatory polypeptide is displayed on, bound to, or contained within said spore.

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35. The composition of claim 30, wherein said at least one antigen is selected from the group comprising peptides, polypeptides, proteins, carbohydrates, or nucleotide sequences of interest.

36. The composition of claim 30, wherein said at least one antigen is a fusion  
30 protein comprising a spore coat polypeptide.

37. The composition of claim 30, wherein said at least one adjuvant is a fusion protein comprising a spore coat polypeptide.

5 38. The composition of claim 30, wherein said at least one co-stimulatory polypeptide is a fusion protein comprising a spore coat polypeptide.

39. The composition of claim 30, wherein said composition further comprises a carrier.

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40. The composition of claim 39, wherein said carrier is a fluid.

41. The composition of claim 39, wherein said carrier is an excipient.

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42. A method for releasing a spore system of interest, said method comprising:  
a) transforming a cell that is capable of sporulation with an exogenous nucleic acid molecule;

b) inducing sporulation of the cell, whereby at least one spore system is produced, said spore system comprising said nucleic acid molecule and/or any polypeptide produced therefrom, and a spore; and

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c) lysing the cell to release said spore system.

43. The method of claim 42, wherein said exogenous nucleic acid molecule encodes a polypeptide.

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44. The method of claim 43, wherein said polypeptide is displayed on or bound to a surface of the spore.

45. The method of claim 43, wherein said polypeptide is contained within said spore.

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46. The method of claim 43, wherein the polypeptide is a fusion protein comprising a spore coat protein of the spore.

47. The method of claim 42, wherein said cell that is capable of sporulation is  
5 a bacterial cell.

48. The method of claim 42, wherein said cell that is capable of sporulation is a fungal cell.

10 49. The method of claim 48, wherein said fungal cell is a yeast cell.

50. A method for displaying a polypeptide at one or more sites of interest on a surface of a spore, said method comprising:

- 15 a) transforming a cell that is capable of sporulation with a recombinant nucleic acid vector comprising a nucleic acid molecule encoding a polypeptide fused in frame to a nucleic acid molecule encoding a spore coat protein; and
- b) expressing a fusion protein comprising said polypeptide and said spore coat protein such that said fusion protein is attached to the spore coat of the spore at one or more sites of interest on the surface of the spore.

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51. The method of claim 50, wherein said spore coat protein is selected from the group consisting of: CotA, CotB, CotC, CotD, CotE, CotF, CotG, CotN, CotS, CotT, CotV, CotW, CotX, CotY, and CotZ.

25 52. A detection system comprising a spore system wherein said spore system comprises a moiety that provides a detectable signal and a polypeptide displayed on, bound to, or contained within the spore system, wherein said polypeptide is capable of capturing a detectable compound.

53. The detection system of claim 52, wherein said polypeptide is selected from the group consisting of: an antibody, a ligand, an antigen, a receptor, an epitope, and an enzyme.

5 54. The detection system of claim 52, wherein said moiety is comprised of a chromophore or fluorophore.

10 55. A method for detecting a compound, said method comprising contacting the detection system of claim 52 with the compound of interest.

56. The method of claim 55, wherein said compound is selected from the group comprising: an enzymatic substrate, an antibody, an antigenic agent, a ligand, and an antagonist.

15 57. A method for delivery of a polypeptide of interest, said method comprising:

a) transforming a cell that is capable of sporulating with a nucleic acid sequence encoding said polypeptide;

b) inducing sporulation of said cell to form a spore; and

20 c) delivering said spore to a site of interest.

58. The method of claim 57, wherein said polypeptide is displayed on or bound to the surface of said spore.

25 59. The method of claim 57, wherein said polypeptide is contained within said spore.

60. The method of claim 57, wherein said spore is delivered as an intact spore.

30 61. The method of claim 57, wherein said spore is delivered as a germinated spore.

62. The method of claim 57, wherein said spore is delivered as a replicating vegetative cell arising from a spore.

5 63. The method of claim 57, wherein said polypeptide is expressed as a fusion protein with a spore coat protein.

64. The method of claim 63, wherein said spore coat protein is selected from the group consisting of: CotA, CotB, CotC, CotD, CotE, CotF, CotG, CotN, CotS, CotT,  
10 CotV, CotW, CotX, CotY, and CotZ.

65. A method for generating a desired product comprising reacting a substrate with a spore system, said spore system comprising a recombinant spore having at least one polypeptide wherein said polypeptide has enzymatic activity.

15 66. The method of claim 65, wherein said spore comprises the enzymes needed to produce said desired product.

67. A composition comprising a spore system said spore system comprising a  
20 recombinant spore having at least one exogenous polypeptide wherein said polypeptide has enzymatic activity and a substrate wherein said enzyme alters said substrate.

68. A composition comprising a spore system, said spore system comprising a non-viable spore and at least one exogenous nucleic acid, peptide, or polypeptide  
25 displayed on, bound to, or contained within said spore.

69. The composition of claim 68, wherein the nucleic acid, peptide, or polypeptide is displayed on or bound to the surface of the spore.

30 70. The composition of claim 68, wherein the nucleic acid, peptide, or polypeptide is contained within the spore.



71. The composition of claim 68, wherein said spore system comprises more than one exogenous nucleic acid, peptide, or polypeptide associated with said spore.

5 72. The composition of claim 68, wherein at least one of said polypeptide has an enzymatic activity.

73. The composition of claim 68, wherein said composition further comprises a substrate which is capable of being altered by said enzymatic activity.

10 74. The composition of claim 68, wherein said spore system is immobilized by attachment to a solid support.

15 75. The composition of claim 74, wherein said solid support is selected from the group consisting of: beads, membranes, gels, microtiter plates, or vessels.

76. The composition of claim 68, wherein said composition further comprises a carrier.

20 77. The composition of claim 76, wherein said carrier is a fluid.

78. The composition of claim 76, wherein said carrier is an excipient.

25 79. A composition comprising a spore system, said spore system comprising a non-viable spore and one or more expression cassettes, wherein said one or more expression cassettes comprise a promoter operably linked to a nucleotide sequence of interest.

30 80. A composition of claim 79, wherein said nucleotide sequence of interest is operably linked to a nucleotide sequence encoding a spore coat protein.

81. A composition of claim 80, wherein said spore coat protein is selected from the group consisting of CotA, CotB, CotC, CotD, CotE, CotF, CotG, CotN, CotS, CotT, CotV, CotW, CotX, CotY, and CotZ.

5 82. A composition of claim 79, wherein the polypeptide encoded by the nucleotide sequence of interest is targeted to the spore coat.

83. A method for modulation of an adjuvant effect in an organism, said method comprising:

- 10 a) generating a non-viable spore, wherein said spore has an adjuvant effect;
- b) isolating said spore; and
- c) contacting said organism with said spore and a nucleic acid, peptide, or polypeptide.

15 84. The method of claim 83, wherein said spore is a recombinant spore.

85. The method of claim 83, wherein said spore is a non-recombinant spore.

20 86. A composition comprising a spore system, said spore system comprising a non-viable spore and one or more expression cassettes, wherein said expression cassettes are comprised of a promoter operably linked to a multiple cloning site.

25 87. A composition of claim 86, wherein said multiple cloning site is operably linked to a nucleotide sequence encoding a spore coat protein.

88. A composition comprising a spore system, said spore system comprising a spore and at least one streptavidin or avidin molecule displayed on or bound to said spore.

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89. The composition of claim 88, wherein said spore of said spore system is a non-viable spore.

5 90. The composition of claim 88, wherein said composition is immobilized by attachment to a solid support.

91. The composition of claim 90, wherein said solid support is selected from the group consisting of: beads, membranes, gels, microtiter plates, or vessels.

10 92. The composition of claim 88, wherein said streptavidin or avidin molecule is a fusion protein with a spore coat protein.

15 93. A composition comprising a spore system, said spore system comprising a spore and at least one exogenous nucleic acid binding particle displayed on or bound to said spore.

94. The composition of claim 93, wherein said spore of said spore system is non-viable.

20 95. The composition of claim 93, wherein said nucleic acid binding particle is selected from the group consisting of peptides, polypeptides, proteins, or nucleic acid molecules.

25 96. The composition of claim 95, wherein said polypeptide is selected from the group consisting of HU and polylysine.

97. The composition of claim 93, wherein said nucleic acid binding particle is a fusion protein comprising a spore coat protein.

30 98. A composition comprising a spore system, said spore system comprising a spore and at least one peptide, polypeptide, protein, carbohydrate, or nucleotide

sequence having anti-pathogenic activity displayed on, bound to, or contained within said spore.

5           99.     The composition of claim 98, wherein said spore of said spore system is non-viable.

          100.    The composition of claim 98, wherein said peptide, polypeptide, or protein having anti-pathogenic activity is a fusion protein comprising a spore coat protein.

10           101.   A method of enhancing an immune response to an immunogenic polypeptide or peptide in a subject, said method comprising administering to the subject a population of spores and an expression vector comprising a nucleotide sequence encoding the immunogenic polypeptide or peptide, wherein the immune response is enhanced compared to the immune response generated by administration of the  
15           expression vector or encoded immunogenic polypeptide or peptide alone to the subject.

          102.    The methods of claim 101, wherein the immunogenic polypeptide or peptide comprises an antigen.

20           103.    The method of claim 101, wherein the enhanced immune response comprises increased antibody production.

          104.    The method of claim 101, wherein the population of spores comprises non-viable or non-germinating spores.

25           105.    The method of claim 101, wherein the spores have an adjuvant effect.

          106.    A method of enhancing an immune response to an immunogenic polypeptide or peptide in a subject, said method comprising administering to the subject  
30           a population of spores and an immunogenic polypeptide or peptide, wherein the immune response to the immunogenic polypeptide or peptide is enhanced compared to the

immune response generated by administration of the immunogenic polypeptide or peptide alone to the subject.

5 107. The method of claim 106, wherein the enhanced immune response comprises an increased production of antibodies specific to the immunogenic polypeptide or peptide.

10 108. The method of claim 107, wherein the immunogenic polypeptide or peptide is an antigen.

109. The method of claim 106, wherein the population of spores comprises non-viable or non-germinating spores.

15 110. The method of claim 106, wherein the spores act as adjuvants to enhance the immune response.

20 111. A composition comprising a spore system, said spore system comprising at least two spores wherein each spore displays a different peptide, polypeptide, or protein.

112. The composition of claim 111, wherein said spore is non-viable.

25 113. The composition of claim 111, wherein said polypeptide is a fusion protein comprising a spore coat protein.

114. The composition of claim 111, wherein said polypeptide is selected from the group consisting of: antigens, adjuvants, co-stimulatory agents, and immunomodulatory agents.

30 115. The composition of claim 111, wherein said spore system modulates more than one immune response in an organism.

116. The composition of claim 115, wherein said immune responses are to different antigens.

5 117. A composition comprising a spore system, said spore system comprising a spore and at least one rotavirus capsid protein displayed on, bound to, or contained within said spore.

10 118. The composition of claim 117, wherein said rotavirus capsid protein is selected from the group consisting of: VP4, VP6, and VP7.

119. The composition of claim 118, wherein said rotavirus capsid protein is VP6.

15 120. The composition of claim 117, wherein said spore is non-viable.

121. The composition of claim 117, wherein said spore system modulates an immune response when administered to an organism.

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